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Recurrent transient thyrotoxicosis in multinodular goitre

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Summary: A patient initially presented with an autonomously functioning right thyroid nodule and transient hyperthyroidism which lasted for a few months. Several months after resolution of thyrotoxicosis, the patient had a recurrent episode of hyperthyroidism and was found to have a left hot nodule. The right hyperfunctioning nodule had become cold on scintigraphy, and its aspiration revealed haemorrhagic fluid suggesting haemorrhagic infarction as the mechanism of resolution of the first episode of hyperthyroidism. Again following resolution of the second episode of hyperthyroidsim, the left hot nodule also became hypofunctioning on scintigraphy indicating that the spontaneous restoration to euthyroidism was secondary to infarction.

Recurrent hyperthyroidism and resolution due to nodular infarction in a patient with a nodular goitre may mimic the more common causes of transient thyrotoxicosis and should be considered in the differential diagnosis of goitrous hyperthyroidism.

Introduction

Plummer's disease represents a heterogeneous spectrum of thyroid anatomical abnormalities ranging from a single autonomously functioning nodule to multiple hyperfunctioning nodules. Patients with this condition may be either euthyroid or thyrotoxic on presentation. The evolution of the disease is also variable and hyperthyroidism may complicate an autonomously functioning nodule as toxic thyroid nodules may undergo regression leading to restoration of euthyroidism.[1] The progression from euthyroidism to hyperthyroidism in patients with autonomously functioning nodules is not very common,[2] and its mechanism is often unclear, although may be related to iodine deficiency or excess.[3-5] Acute haemorrhagic infarction of the nodule may cause a transient thyrotoxic state of short duration,[6] may account for the regression of the hyperthyroidism, and often results in the formation of a cold nodule replacing the preexisting hyperfunctioning nodule. Degeneration of a nodule without overt haemorrhagic infarction also may cause regression of the thyrotoxicosis in nodular toxic goitre.[7] We report here a patient with recurrent transient hyperthyroidism due to a nodular goitre in whom the resolution of the hyperthyroid state is due to infarction of the hyperfunctioning nodules on both occasions.

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Case report

A 60 year old black female presented in March, 1983 with a two-month history of heat intolerance and a 35 pound weight loss, but denied diarrhoea, eye symptoms, or palpitations. On physical examination, the blood pressure was 160/80 mmHg, the pulse rate was 108/minute and regular, temperature 37°C. There was a 3 × 2 cm thyroid nodule in the right lobe, non-tender and not associated with lymphadenopathy. The left lobe of the thyroid was normal. There was a fine tremor of the hands and slightly decreased proximal muscle strength. The skin was moist and the ankle jerk relaxation time was slightly diminished. Total thyroxine (T4) by RIA was 234.2 nmol/l (normal = 54 – 122.2); triodothyronine (T3) resin uptake, 37% (normal = 25%–35%); free thyroxine index, 16.7 (normal = 5.5–11.5). The 24 hour radioactive iodine uptake was 51% (normal = 7–32%) and the thyroid scan showed a right hyperfunctioning thyroid nodule, with partial suppression of the remaining gland (Figure 1a). She progressively became less symptomatic, and 6 months after initial presentation, she was entirely asymptomatic and was clinically euthyroid. On examination there was a thyroid nodule measuring 2.5 cm in the right lobe. T4 was 142.85 nmol/l, T3 resin uptake was 28%, free T4 was 25.7 pmol/l (normal = 11.6–23.1), and T3RIA was 3.14 nmol/l (normal = 1.15–3.07). The patient was seen again 5 months later and was found to be clinically and biochemically euthyroid. Subsequently she remained asymptomatic until May, 1985.

In June, 1985 the patient presented again with a 4-week history of heat intolerance and palpitations. She was clinically hyperthyroid with warm, moist skin. There was a 3 cm × 4 cm thyroid nodule noted on the left and a 2.5 cm × 3 cm nodule on the right. The total T4 was 207 nmol/l, T3 3.22 nmol/l and the 24-hour radioactive iodine uptake was 49%. A repeat thyroid scan showed a cold nodule in the right lobe and a new hyperfunctioning nodule on the left side (Figure 1b). A fine needle aspiration biopsy of the cold nodule revealed a haemorrhagic material. In September, 1985, serum T4 was 176.3 nmol/l, T3RIA 3.53 nmol/l, T3 resin uptake 29%. Subsequently, she gradually felt better and did not return for follow-up until 1 year later when she was again found to be clinically euthyroid. The nodules were 2 × 3 cm on the right and 2 × 2 cm on the left side. The thyroid function tests were again normal, and the thyroid scan showed 2 areas of decreased radioactive iodine uptake in both thyroid lobes. A fine needle aspiration biopsy of the left nodule also revealed a haemorrhagic material.

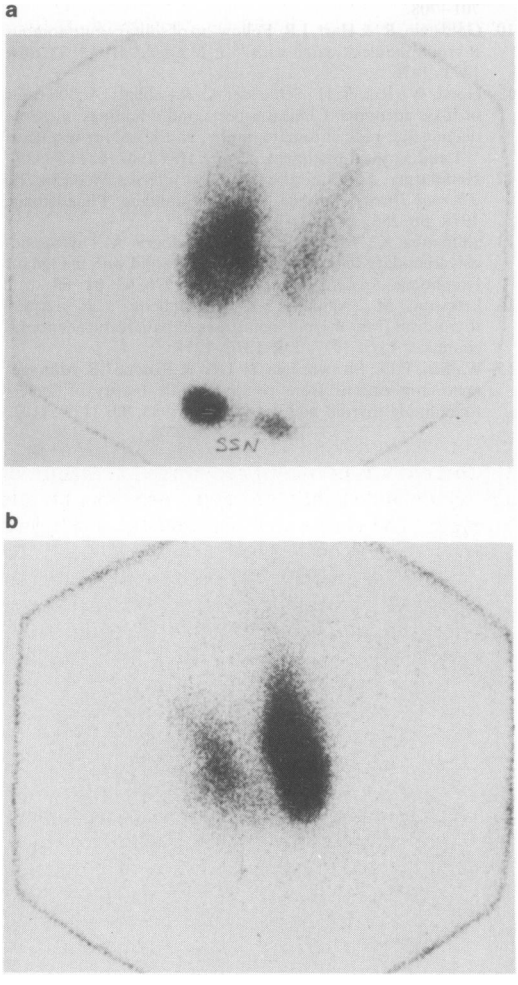

Figure 1 Scintigraphic findings of the thyroid gland when the patient experienced (a) the first and (b) the second episode of thyrotoxicosis.

Discussion

The initial presentation in our patient was that of a single right autonomously functioning nodule associated with thyrotoxicosis that resolved spontaneously within a few months. The natural history of an autonomous thyroid nodule is variable. Untreated, hyperfunctioning, non-toxic nodules usually remain stable, may slowly progress to become larger causing thyrotoxicosis, or may undergo spontaneous resolution.[7-9] Transformation of the autonomously functioning nodule to a hypofunctioning one may also occur following radioactive iodine therapy.[10,11] In general, the occurrence of hyperthyroidism in non-toxic hyperfunctioning thyroid nodules has been considered rare. In many patients, the pathogenic factors implicated have been iodine deficiency or excess and haemorrhagic infarction.[3-6] The latter is often but not always associated with local pain and tenderness. Our patient has not resided outside of the Houston area, has not experienced any neck symptoms during either period of transient thyrotoxicosis, and the thyroid scans showed an increased radioactive iodine uptake during the hyperthyroid phase, suggesting that the haemorrhagic infarction of both nodules was not the mechanism of the hyperthyroidism but rather the mechanism of its resolution.

The occurrence of a second left autonomous nodule after transformation of the first nodule suggests that the goitre progressed from a single nodular goitre to a multinodular goitre. This type of evolution is not uncommon.[5] One of the unusual features in our patient is that the second autonomously functioning nodule also led to a short-lived thyrotoxicosis that lasted only a few months. Transient hyperthyroidism often raises the possibility of subacute thyroiditis or lymphocytic thyroiditis with resolving hyperthyroidism. These types of thyroiditis cause disruption and destruction of the follicular architecture responsible for excessive release of thyroid hormone into the circulation. The transient thyrotoxicosis often subsides within a few weeks. Conditions associated with destruction-induced hyperthyroidism were excluded by the finding of an elevated 24-hour radioactive iodine uptake. None of the other causes of transient hyperthyroidism such as extensive infiltration of the thyroid gland by lymphoma[12,13] or adenocarcinoma[14] were substantiated.

In the patient described, auto-ablation caused by a haemorrhagic process might have prevented the nodules from remaining permanently toxic. The most definite evidence for degeneration and autodestruction of the hyperfunctioning nodule was the recovery of function in the previously suppressed contralateral thyroid lobe. Furthermore, the finding of blood in the needle aspiration biopsy, in conjunction with the nature of the nodule makes the diagnosis of haemorrhagic infarction obvious. To our knowledge, this is the first documented case of recurrent transient thyrotoxicosis in a patient with multinodular goitre. The conservative, non-surgical management of patients with this entity should include close follow-up for occurrence of autonomy and hyperthyroidism. Furthermore, fine needle aspiration biopsy, usually not very reliable in the presence of a hyperfunctioning nodule,[15] may be an important diagnostic tool when the nodule becomes hypofunctioning on thyroid scintigraphy.

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